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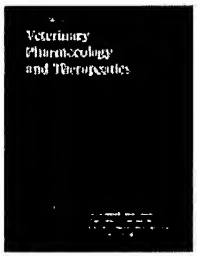

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Original Article

Characterization of vasodilatory adenosine receptors in equine digital veins

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Abstract

Isolated equine digital veins (EDVs) which had been denuded of their endothelium were used to study adenosine receptors causing vasodilation. When the blood vessel wall tension was raised with the thromboxanemimetic, U44069 (30 n M), the order of vasodilator potency of adenosine receptor agonists was: 5'-N-ethylcarboxamidoadenosine (NECA) > 2-*p*-(2-carboxyethyl)phenyl amino-5'-N-ethylcarboxamido-adenosine (CGS 21680) > 5'-N-methylcarboxamido-adenosine (MECA) >> N^6-cyclohexyladenosine (CHA) > N^6-cyclopentyladenosine (CPA) > N^6–2-(4-Aminophenyl) ethyladenosine (APNEA) > adenosine. Removal of the endothelium had no significant effect on the responses to NECA. The adenosine receptor antagonists, 8-cyclopentyl-1,3-dipropylxanthine (DPCPX; A_1-selective) and xanthine amine cogener (XAC; non-selective

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Adenosine A1 Receptors Mediate Retinotectal Presynaptic Inhibition: Uncoupling by C-Kinase and Role in LTP During Regeneration

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ABSTRACT

Zhang, Chunyi and John T. Schmidt. Adenosine A1 receptors mediate retinotectal presynaptic inhibition: uncoupling by C-kinase and role in LTP during regeneration. *J. Neurophysiol.* 79: 501-510, 1998. Presynaptic adenosine receptors inhibit transmitter release at many synapses and are known to exist on retinotectal terminals. In this paper we show that adenosine decreases retinotectal field potentials by ~30% and investigate the mechanism. First, as judged by the effects of specific calcium channel blockers, retinotectal transmission was mediated almost exclusively by N-type calcium channels, which are known to be modulated by adenosine A1 receptors. Transmission was completely blocked by either ω-Conotoxin GVIA (−100%, N-type blocker) or ω-Conotoxin MVIIC (−99%, N-, P- and Q-type blocker) and was not significantly affected by ω-Agatoxin IVA [+1.7 ± 9.3% (SE), P-,Q-type blocker], but was augmented slightly by nifedipine(+9.3 ± 2.1%, L-type blocker). Second, the adenosine inhibition was presynaptic, as indicated by a 43% increase in paired-pulse facilitation. Third, the selective A1 agonist cyclohexyl adenosine (CHA) at 50 nM caused a 21% decrease in amplitude and the selective A2 agonist N^6-[2-(3,5-dimethoxyphenyl)-2-(2-methylphenyl)-ethyl]adenosine (DPMA) at 100 nM caused a 24% increase. Fourth, the selective A1 antagonist 8-cyclopentyl-1,3-dipropylxanthine (DPCPX) alone produced an increase in the field potential, suggesting a tonic inhibition mediated by endogenous adenosine. Fifth, pertussis toxin eliminated adenosine inhibition implicating G_i or G_o protein coupling. Sixth, C-kinase activation eliminated the A1-mediated inhibition. In regenerating projections, adenosine also caused a decrease in transmission (−30 ± 12%), but after induction of long-term potentiation (LTP) via trains of stimuli or via treatment with the phosphatase inhibitor okadaic acid, the adenosine response was converted to an augmentation. Because LTP is associated with C-kinase activation, this is consistent with C-kinase uncoupling the A1 receptor from inhibiting

Journal Article

Effects of several 5′-carboxamide derivatives of adenosine on adenosine receptors of human platelets and rat fat cells

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Summary The effects of several 5′-carboxamide derivatives of adenosine on stimulatory (R_a) adenosine receptors of human platelets and inhibitory (R_i) adenosine receptors of rat fat cells have been compared. 5′-N-Cyclopropylcarboxamidoadenosine (CPCA) and 5′-N-ethylcarboxamidoadenosine (NECA) most potently inhibited ADP-induced aggregation of human platelets as shown by IC_{50}-values of 0.24 and 0.34

μmol/l. 5′-N-Methylcarboxamidoadenosine (MECA; IC_{50} 0.81 μmol/l) and 5′-N-carboxamidoadenosine (NCA; IC_{50} 2.1 μmol/l) were less potent, whereas adenosine, 2-chloroadenosine and (-) N^6-phenylisopropyladenosine [(-)PIA] exhibit IC_{50}-values of about 1.5 μmol/l. Nearly the same rank order of potency was obtained for stimulation of adenylate cyclase activity of platelet membranes and for inhibition of [^{3}H] NECA binding to human platelets. In order to examine the effects of the carboxamide analogues on R_i adenosine receptors of rat fat cells inhibition of lipolysis and adenylate cyclase were studied. (-)PIA was the most potent inhibitor of lipolysis as shown by an IC_{50} of 0.5 nmol/l, followed by CPCA (IC_{50} 1.1 nmol/l) and NECA (IC_{50} 1.3 nmol/l), whereas MECA (IC_{50} 17.9 nmol/l) and NCA (IC_{50} 20.1 nmol/l) were much less potent than NECA in inhibiting lipolysis. Similar results were obtained for inhibition of adenylate cyclase activity of fat cell membranes and for competition with [^{3}H]PIA binding to fat cell membranes. The relative potencies of the adenosine analogues at both receptor subclasses were calculated from the ratio of the IC_{50}-values for inhibition of platelet aggregation and of lipolysis. (-)PIA showed the highest selectivity for R_i receptors as indicated by a 2,900-fold lower IC_{50} for the antilipolytic than for the antiaggregatory effect. The R_a/R_i activity ratio for NECA was about 260, for CPCA 220, for NCA 105 and for MECA 45. These results indicate that all 5′-carboxamide adenosine derivatives are more potent agonists at R_i receptors than at R_a receptors. Since MECA has a higher

Development of A2A Adenosine Receptor Agonists and Antagonists. *ChemMedChem* [CrossRef]
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NMDA-Independent LTP by Adenosine A_2 Receptor-Mediated Postsynaptic AMPA Potentiation in Hippocampus

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ABSTRACT

Kessey, Kofi and David J. Mogul. NMDA-independent LTP by adenosine A_2 receptor-mediated postsynaptic AMPA potentiation in hippocampus. *J. Neurophysiol.* 78: 1965-1972, 1997. The role of adenosine A_2 receptors in normal synaptic transmission and tetanus-induced long-term potentiation (LTP) was tested by stimulation of the Schaffer collateral pathway and recording of the field excitatory postsynaptic potential (EPSP) in the CA1 region of rat transverse hippocampal slices. Activation of adenosine A_2 receptors with the A_2 agonist N^6-[2-(3,5-dimethoxyphenyl)-2-(2-methylphenyl)-ethyl]adenosine (DPMA; 20 nM) enhanced synaptic transmission during low-frequency test pulses (0.033 Hz). Paired stimulation before and during DPMA exposure indicated no paired-pulse facilitation as a result of A_2 activation, suggesting that enhancement was not a result of presynaptic modulation. DPMA enhanced the early phase α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) component of the EPSP. In contrast, DPMA had no effect on the *N*-methyl-D-aspartate (NMDA) component isolated using low extracellular Mg^{2+} and the AMPA receptor blocker 6-cyano-7-nitroquinoxaline-2,3-dione (20 μM), indicating that the effects of A_2 activation on synaptic transmission were mediated by a postsynaptic enhancement of the AMPA response. Activation of adenosine A_2 receptors during a brief tetanus (100 Hz, 1 s) increased the level of LTP by 36% over that seen in response to a tetanus under control conditions. DPMA exposure after prior induction of LTP showed no additional potentiation, indicating that the mechanisms that contribute to both types of increases in synaptic transmission share a common mechanism. A slow onset NMDA-independent LTP could be induced by application of a tetanus during perfusion of DPMA with the NMDA blocker AP5 (50 μM).